the kidney pelvis and ureters, with masses of acetylsulfapyridine crystals. The first indication of this serious condition may be abdominal pain from ureteral colic, numerous blood cells in the urine, or frank hematuria. Some degree of hematuria is said to occur in 5 per cent of cases receiving sulfapyridine. If this is generally true, we must have overlooked it a number of times. Azotemia may occur, and any sudden drop in the urinary output demands prompt investigation. Cases have been reported in which kidney function was reestablished and the patient's life saved by ureteral lavage.

PNEUMONIA SERVICES AT LOS ANGELES GENERAL HOSPITAL

In the year 1939 three hundred thirty-one adults with pneumococcus pneumonia were treated with chemotherapy, serum or both, on the two Pneumonia Services at the Los Angeles General Hospital, with a mortality of 13 per cent, the lowest rate for this hospital since satisfactory records have been kept. The first four months of 1940 have shown a further drop in mortality to approximately 10 per cent.

OTHER PNEUMONIAS

What has been said up to this point applies only to the pneumonias in which the pneumococcus is the infecting organism. The time allowed me will permit only brief mention of the results with chemotherapy in the pneumonias of other etiology.

Fair results have been reported from the use of sulfanilamide and sulfapyridine in hemolytic streptococcus pneumonias. We have seen little or no benefit in streptococcus viridans infections.

Sulfamethylthiazole is said to be efficacious in staphylococcus infections, but in four staphylococcus pneumonias recently observed—one with a positive blood culture—this drug seemed to be of little value until polyvalent staphylococcus antitoxin was added to the treatment. All four of these patients recovered. Because of the frequency of multiple neuritis following the use of sulfamethylthiazole it will probably not be released for general distribution.

We have had no experience with tularemic pneumonia, but Richards of Salt Lake City has recently reported that sulfanilamide is of benefit in these cases.

A few scattered reports on the treatment of Friedlander's infection with chemotherapy have recently appeared and are most encouraging. In the past few months we have treated, with sulfapyridine, three Friedlander's pneumonias, one with a strongly positive blood culture and one with cavitation. All three were desperately ill. All recovered.

As might be expected, virus pneumonias do not seem amenable to chemotherapy.

IN CONCLUSION

In summary, it can safely be said that chemotherapy is of definite value in nearly all types of pneumonia. When judiciously used alone, or in conjunction with specific serum, it has resulted in a remarkable reduction in the mortality from pneumococcus pneumonia. I venture to predict that within a year the death rate from this disease, even in our large charity hospitals, will drop below 10 per cent; and pneumonia, instead of ranking fourth among the causes of death, will be pushed far down the list.

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SURGICAL TREATMENT OF ESSENTIAL HYPERTENSION*

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THE medical treatment of progressive essential hypertension, in most instances, has been so unsuccessful in the past that it is only natural that surgical procedures for the relief of this grave condition should have been added to our therapeutic armamentarium. These surgical procedures have been employed for a sufficient length of time for us to estimate their efficacy and evaluate the results. Statistical data thus far show the mortality to be extremely low, that there is no resultant disability of any consequence, and that the clinical results in a certain percentage of selected cases have been of great value.

The importance of the work, study, and accumulated experimental and clinical evidence that has been compiled is apparently underestimated by the profession as a whole. Just why this should be it is difficult to say. True, all new surgical procedures, and especially those that are extensive in character, are, and should be, looked upon with a certain amount of healthy constructive skepticism. In the light of the clinical data at hand on this subject, however, it is hard to explain the antagonism which is displayed by a large section of the profession toward these newer procedures.

Every physician knows that the medical treatment of progressive essential hypertension, with the exception of those cases sensitive to potassium sulphocyanate, has been anything but satisfactory. If anyone doubts this, let him consult the files of the ever-increasing number of physicians who themselves are submitting to surgical relief of hypertension. Why, then, condemn some new method of approach because the results are not 100 per cent perfect? I am quite sure that most physicians would be pleased if they could get the results medically that have been and are being obtained with surgery. We do not hesitate to recommend surgical procedures in the therapy of cancer if there is the slightest hope of operability. Progressive hypertension is just as dangerous and much more prevalent than cancer. It is not logical to deny these people what relief surgery may offer.

THEORETICAL CONSIDERATIONS

The true cause of primary essential hypertension is not as yet known. We do not presume to state, therefore, that we can remove the cause and cure hypertension surgically, any more than we can state

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that surgical removal will cure cancer. We do presume to state, however, that we can arrest a certain percentage of cases of hypertension by surgery, just as we do in malignancy.

Cannon[1] many years ago showed that in surgical shock a drop in blood pressure followed vasodilatation of the splanchnic vascular bed. Conversely, stimuli applied to the splanchnic nerves cause a vasoconstriction of this area with a corresponding rise in blood pressure. Goldblatt[2] has shown by brilliant animal experimentation that hypertension can be produced by gradual mechanical constriction of the renal arteries. It is possible that, in man, vasoconstriction of the kidney arterioles, a neurogenic clamp so to speak, is a corollary to Goldblatt's experiments. The theory of a pressor substance being elaborated in these ischemic kidneys, while possible, has not yet been definitely proved. And, lastly, there is the theory of hyperfunction of the adrenal glands, evidence at hand being against it.

Thus we do not know whether the cause of hypertension is a hyperactive vasomotor mechanism, whether it is a truly arteriolar disease *per se,* whether it is a pressor substance circulating in the blood, or whether it is the factor of hyperadrenalism. Regardless of the cause, however, we do know that the fundamental mechanical reason for elevation in blood pressure is the increased resistance offered to the flow of blood through the peripheral vessels.

SURGICAL APPROACH

Surgery attempts to decrease this arteriolar resistance by denervation of the splanchnic area, the renal vessels and kidneys, and the adrenal glands, together with a large part of the lower extremities by the subdiaphragmatic operation. That it does so has been demonstrated in many cases.

Peet,[3] in 1934, was the first to do bilateral resection of the splanchnic nerves above the diaphragm, and he has had the largest experience with this type of operation. Craig and Adson[4-7] developed the procedure of splanchnic resection below the diaphragm and have done many hundreds of cases. The Criles[8] have performed celiectomy in a large series. All of these procedures aim to attain the same result, namely, vasodilatation of the splanchnic bed, the kidneys, and the adrenals. Allen and Adson[9] have answered many of the theoretical objections to sympathectomy. The surgical approach, then, is physiologic and not pathologic in character. We are not attempting to remove the cause of hypertension because we do not know the cause.

SELECTION OF CASES

The selection of cases is of the utmost importance. In our experience, at least, it is the crux of the whole procedure. We must first be sure that we are dealing with primary essential hypertension and not secondary hypertension due to specific causes. Secondary hypertension has been estimated by Allen and Adson[10] to include about 15 per cent of hypertensives and their classification of causes is: coarctation of the aorta, glomerulonephritis, suprarenal tumor, hyperthyroidism, arteriovenous fistula, and aortic heart disease. It is mandatory that these entities be ruled out and a diagnosis made of primary essential hypertension, which will comprise about 85 per cent of the cases.

Granted, then, that we are dealing solely with cases of primary elevations of pressure. It must be self-evident that if a marked degree of arteriosclerosis is present, with blood-pressure readings fixed at high levels with or without marked kidney damage and impairment of renal function, any operation based on the principle of sympathectomy will certainly be futile. It has seemed to us that the criteria adopted by Craig and Adson[4] are both conservative and reasonable. They are:

I. There has been no response to competent medical treatment. (We ourselves stress the failure of sulphocyanate therapy.)

II. Patients approximately fifty years of age or under. (This, however, is relative.)

III. There should be no marked arteriosclerosis as determined by eye-ground findings.

IV. There should be a minimal amount of kidney damage present.

V. Blood pressures should be labile and not fixed at high levels. Our routine procedure is as follows:

1. The patient is put at absolute bed rest in the hospital. Hourly blood-pressure readings are taken day and night for the first twenty-four to forty-eight hours. Flothow[11] has made the observation, and our experience has confirmed his, that those patients who show a marked drop in both systolic and diastolic pressure under the influence of natural sleep have a much better chance of a good result.

2. The reaction to the well-known cold pressor test is taken. Preferably a sharp rise in pressure should occur, followed quickly by a sharp drop to former levels.

3. Kidney function tests are done by the standard methods, but particular importance is placed on the Fishberg concentration test. Peet and others feel that a low level of urine concentration mitigates against a good result.

4. Eye-ground examination is done by competent ophthalmologist. There should be a minimal amount of arteriosclerosis present, although retinal hemorrhage is not a contraindication.

5. With the patient at rest, one-half grain of sodium nitrite is given by mouth every one-half hour for six doses and the blood-pressure readings recorded at thirty-minute intervals. There should be a drop in pressure.

6. The basal pressure is taken and 2.5 per cent sodium pentothal administered intravenously until the patient is in deep narcosis. There should be a profound drop in pressure under the action of this powerful barbiturate.

If, then, we have a patient who shows a marked lability of pressure and, particularly, one who will show a marked drop during sleep, who has minimal eye-ground changes and a good kidney function, we believe that patient to be a candidate for surgery.

In this regard it may be stated that our own personal experience has made us more and more critical in our selection of cases. Most of our poor

results have been in cases that we accepted previously which we would turn down today. As in most other things, experience is a great teacher. Suffice it to say that the younger the patient the more labile the blood pressure, and the less permanent permanent cardiovascular renal damage present the more hopeful the outlook.

CONTRAINDICATIONS

Craig[6] states that contraindications for surgery are (*a*) congestive heart failure, (*b*) coronary occlusion, (*c*) marked nephritis, and (*d*) arteriosclerosis. Retinitis, moderate heart enlargement, slight renal damage and cerebral accidents in which recovery has taken place, are not contraindications.

TECHNICAL PROCEDURE

We have adopted from the start the Craig-Adson operation which has been described many times. It consists in removal of the greater, lesser and least splanchnic nerves, together with all or part of the celiac ganglia, together with the first and second lumbar ganglia. Theoretically, at least, this should cause a vasodilatation of the splanchnic bed, the renal arteries, kidneys, adrenals, and the greater part of the lower extremities. It has the disadvantage of being a two-stage procedure, each side being done about ten days apart. It seems to be a little safer than Peet's operation, which is a one-stage supradiaphragmatic removal of the splanchnic nerves. It has the advantage of our being able to explore the adrenals and also to remove the upper lumbar ganglia. From statistical data, however, the results seem to be about the same in both types of procedures.

COMPLICATIONS

There is no resultant disability of any consequence. Some patients develop an orthostatic hypotension which can be corrected with an abdominal belt. Some develop a temporary effort tachycardia which can be controlled by moderate limitation of activity. There is no disturbance of urination, defecation, or menstrual function. There is no interference with sexual function except that males are sterile because there is no longer a discharge of semen. Libido and potentia are preserved. The sweating function of the lower extremities is abolished and there is a slight rise in skin temperature in these regions.

RESULTS

Upon those of us doing this work, it is more and more being impressed that results should be measured not alone by postoperative blood-pressure levels, but also by relief of clinical symptoms. Measured alone by blood-pressure levels, the results are inconstant. Measured by clinical symptoms, such as headache, dizziness, fatigue, precordial pain, etc., the results in a large percentage of cases are excellent. Why this is so it is difficult to say. Crile has advanced the theory that sympathectomy abolishes the sudden sharp rises in pressure commonly seen in hypertensives, at which time their symptoms and cardiovascular accidents develop. Clinically this seems to be true and, if so, it is of great value.

Peet[12] has reported 194 cases with a follow-up of from six months to five years. His standard of good result, measured by repeated blood-pressure readings maintained over a period of time, is that there must be a drop or 40 millimeters or more systolic and 15 millimeters or more diastolic. Taking all ages and stages of the disease in his 194 patients, a good result was obtained, as measured by the above standard, in 46 per cent. Measured by symptomatic improvement as set forth above, 87 per cent of patients were relieved of practically all symptoms. Of most significance, however, is the fact that 58 per cent, all of whom were completely incapacitated prior to surgery, were returned to useful economic existence and were back at their original jobs.

Craig and Adson,[5] of the Mayo Clinic, have reported 237 cases without an operative death. From a symptomatic standpoint they report relief of headache in 85 per cent, of nervousness in 71 per cent, precordial pain in 75 per cent, and fatigue and dyspnea in 45 per cent. As measured by blood-pressure readings taken six months to several years postoperative, a significant maintained drop in pressure was seen in 52 per cent. Thus it can be observed that their results practically approximate those obtained by Peet.

In our cases we now have careful follow-up records of twelve cases which have gone from six to thirteen months postoperatively. The ages ranged from twenty-four years to fifty-two years, the average age being forty-two years. All were patients who had not been relieved by medical treatment, and most of them had been on sulphocyanate without relief. All had systolic pressures approximately 200 millimeters or over, and diastolic pressures ranging from 110 to 150 millimeters. The operative mortality was nil and there were no postoperative complications of any kind. Nine, or 75 per cent, have been almost completely relieved of their preoperative symptoms and are back at their original occupations. The three who were not relieved were poor selections from the start, and, in the light of our increasing experience, would not be accepted by us today. As measured by follow-up blood-pressure readings, three, or 25 per cent, have maintained pressures below 150 millimeters systolic and 100 millimeters diastolic. Two, or 17 per cent, have had a significant maintained reduction, but not approaching normal. Thus, measured by blood-pressure readings alone, we have a good result so far in 42 per cent of cases.

As time passes and our experience grows, I believe that we shall be able to raise these percentages materially by being more and more critical in our selection of cases. This, I think, is being demonstrated by our most recent ones, which are not included here because of the short length of time postoperative. We believe, and Peet has demonstrated this, that if patients are seen in the younger age limits before material damage has been done to the vascular-renal system, our chances of good results will be measurably increased. What the long-term future results fifteen or twenty years from now will be we do not know, but so far the outlook is hopeful.

SULPHOCYANATE

We feel that all patients should be given an adequate trial with potassium sulphocyanate by mouth before operation is considered. This treatment should be carried out by the method outlined by Barker.[13] There are a number of patients who can be controlled by this drug if the blood cyanate level is kept at from 6 to 12 milligrams per 100 cubic centimeters of blood. If patients are not sensitive to cyanate therapy, we feel that surgery should be considered without delay. Davis and Barker[14] have recently reported an interesting group of individuals who were resistant to sulphocyanate, but who, following sympathectomy, were extremely sensitive to it. Just what takes place here is not known, but it may give us a clue to further relief in some patients who do not get a good result with surgery alone.

IN CONCLUSION

Although sympathectomy is based on physiologic and not pathologic grounds, and is probably not the final answer to the problem, the results to date amply justify its employment in carefully selected cases of hypertension.

Patients with progressive essential hypertension who still have labile pressures and no marked cardiovascular renal damage, and who cannot be controlled medically and particularly with cyanate therapy, have everything to gain and nothing to lose by surgery.

We feel that physicians have a moral responsibility to their patients to investigate these newer procedures and, in case of failure of a medical regime to arrest the disease, to acquaint these individuals with the possibility of relief by surgery.

Wakefield Building.

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CHANGING TREATMENT IN ACUTE INFECTIONS*

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CHANGES in treatment of acute infectious diseases in the past five years include almost the entire field of this type of therapy. With the advent of sulfanilamide and its derivatives, the development of new and better sera, and numerous lesser advances, almost every one of the commoner infectious diseases is now treated in ways radically different from those of a half-decade ago, and the end is not yet. With the huge scope of the subject and the constant change as the new is being tested and the old discarded, the present report will be little more than an outline of conditions at the moment; and it will be further limited to experiences in one large hospital unit for the treatment of these diseases.

SULFANILAMIDE

Sulfanilamide and related compounds obviously have brought the greatest single element of change. The gross mortality rate of the Communicable Disease Unit of the Los Angeles County General Hospital dropped approximately one-third during the first year of use of this remarkable drug; and though other therapeutic advances occurred at the same time, this dramatic change is largely due to sulfanilamide. The more recent development of related compounds, notably sulfapyridine, leads to optimism for the future.

A review of the technique of administration of sulfanilamide seems unnecessary, since it has been so thoroughly and frequently covered in all medical literature. A brief comment on dosage may not be amiss, however, as experience shows that there is still confusion on this subject. In brief, one may say that the proper dose is the dose that cures the patient and that this dose is not the same in all patients nor in all diseases; and, most important, that the dose ultimately must be considered in terms of drug concentration in the blood and not in terms of dosage administered. When a supposedly adequate dose is given in a disease known to respond to the drug and improvement does not occur when it should, a check of blood concentration may provide a clear-cut reason; and blood determinations should be routine in all seriously ill patients. The arbitrary level of 10 milligrams per 100 cubic centimeters is a useful point of departure, but it is not an absolute in any single disease nor is it the ideal concentration for all different diseases. In general, we have found that in the following more common conditions the dose indicated is adequate,

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